

Charles University

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Title of Thesis: Study of cytotoxicity of potential antituberculotics using selected methods on liver and kidney cell line

During pharmacologic therapy, tissues of liver and kidney are frequently exposed to high doses of xenobiotics. Via *in vitro* assays during preclinical testing, we are able to predict potential toxicity which helps to prevent the possible serious adverse drug reactions in clinical practice. The aim of this rigorous thesis was to state the cytotoxic profile of 4 potential antituberculotic drug candidates using appropriate cell models and *in vitro* assays. Another aim was to compare the cytotoxic effect of the tested compounds among themselves and to 4-aminosalicylic acid (PAS) which antituberculotic activity is known for many years. The tested substances were 3 salicylanilide diethyl phosphate-based derivatives and 4-(trifluoromethyl)benzoic acid. For the cytotoxic potential assessment, we used the parameter half maximal inhibitory concentration IC_{50} . We have used methods determining the cell metabolic activity, aminopeptidase activity, lactate dehydrogenase leakage and activity of 3/7 caspases in this experimental work. As the experimental model was chosen human liver (Hep G2) and kidney (HK-2) standard cell lines. In cell viability assays, all tested compounds showed more toxic effect in Hep G2 cells in comparison to HK-2 cells. Salicylanilide diethyl phosphates were in cell viability assays more cytotoxic than 4-(trifluoromethyl)benzoic acid and PAS. The most of the compounds caused lactate dehydrogenase leakage only at higher concentrations. The potential of the compounds to activate caspases in both cell lines was low. As a conclusion could be claimed that by the chosen methods we managed to set IC_{50} parameter of the tested compounds and compared the cytotoxic effects of the tested compounds among themselves and to PAS.